

Curriculum vitae

Name: Tania Crombet Ramos

Date of birth: March 27, 1970.

Birth place: Havana, Cuba.

Nationality: Cuban

Address: B No. 8302 e / 5th and 100, Altahabana, Havana, Cuba.

Languages: English

Current responsibility: Medical Director of the Center of Molecular Immunology

Work center: Center of Molecular Immunology.

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Scientific degree: MD (1993), PhD (2004)

Superior education:

1987-1993: Medical Doctor, Superior Institute of Medical Sciences of Havana

1993-1997: Immunology Specialist, Superior Institute of Medical Sciences of Havana

2004: Philosophical Doctor, Superior Institute of Medical Sciences of Havana

Professional experience:

1993-1997: Residency in Immunology. Superior Institute of Medical Sciences of Havana.

1998-2000: Specialist of the Division of Clinical Immunology. Center of Molecular Immunology (CIM)

2000-2009: Chief of the Division of Clinical Immunology of the Center of Molecular Immunology

2009-today: Medical Director of the Center of Molecular Immunology

1999-2002: Professor of the Latin American School of Medical Sciences.

2015-today: Member of the Board of Directors of Innocimab, a Joint Venture between Singapore and Cuba for the development of nimotuzumab.

2016: Senior Faculty of the Superior Institute of Medical Sciences of Havana.

2017: Member of the Cuban Academy of Sciences.

2018: Member of the Board of Directors of Innovative Immunotherapy Alliance, a Joint Venture between US and Cuba for cancer immunotherapy.

Scientific societies and Scientific Boards

1996-present: Member of the Cuban Society of Immunology

1996-present: Member of the Latin American Society of Immunology

2004-present: Member of the American Society of Clinical Oncology

2008-2014: Member of the Scientific Council of the National Institute of Oncology

2010-present: Member of the Cuban National Group of Oncology

2013-present: Member of the Scientific Council of Biocubafarma. (Biocubafarma is the group that gathers all the Pharmaceutical and Biotechnology Industry of Cuba)

2018-present: Member of the Board of Directors of Innovative Immunotherapy Alliance, first Joint Venture between Cuba-US for the development of cancer immunotherapy.

Publication of more than 100 papers in high impact journal and oral presentation of in more than 200 international congress in Cuba and abroad.

Main publications

1. Gonzalez G, Crombet T, Catala M, Mirabal V, Hernandez JC, Gonzalez Y, Marinello P, Guillen G & A. Lage; A novel cancer vaccine composed of human-recombinant EGF linked to a carrier protein: report of a pilot clinical trial; *Ann Oncol* 1998 Apr;9(4):431
2. Crombet T, Torres O, Neninger E, Catala M, Rodriguez N, Ramos M, Fernández E, Iznaga N, Pérez R and Lage A. ; Phase I clinical evaluation of a neutralizing MAb against EGFR; *Cancer Biother Radiopharm* 2001; 16(1):93.
3. Crombet T, Torres O, Menéndez A, Stevenson A, Ramos M, Torres F, Figueredo J, Veitía I, Iznaga N, Pérez R and Lage A; Phase I clinical evaluation of a neutralizing monoclonal antibody against EGFR in advanced brain tumor patients: preliminary study; *Hybridoma* 2001; 20:131
4. Vilorio-Petit A, Crombet T, Jothy S, Hicklin D, Bohlen P, Schlaeppi JM, Rak J, Kerbel B; Acquired resistance to the antitumor effect of EGFR blocking antibodies in vivo: a role for altered tumor angiogenesis; *Cancer Res* 2001; 61(13):5090
5. Crombet T, Rak J, Perez R and Vilorio A. ; Antiproliferative, antiangiogenic and proapoptotic activity of h-R3: A humanized anti-EGFR antibody; *Int J Cancer* 2002; 101(6):5675.
6. Crombet T, Torres L, Neninger E, Catala M, Solano ME, Perera A, Torres O, Iznaga N, Torres F, Pérez R, Lage A; Pharmacological evaluation of humanized anti-EGFR Mab h-R3, in patients with advanced epithelial derived cancer.; *J Immunother* 2003; 26(2):139.
7. Crombet Ramos T, Casaco Parada A, Iznaga Escobar N.; h-R3: TheraCIM; *Drugs of the future* 2003, 28 (9): 847-853
8. Gonzalez G, Crombet T, Torres F, Catala M, Alfonso L, Osorio M, Neninger E, Garcia B, Mulet A, Perez R, Lage A.; EGF based Cancer Vaccine for Non-Small Cell Lung Cancer Therapy.; *Ann Oncol* 2003; 14(3):461
9. Lage A, Crombet T and Gonzalez G; Targeting EGFR signaling: early results and future trends in oncology.; *Ann Med.* 2003; 35(5):327
10. Crombet T, Pérez R, Lage A, Osorio M, Cruz T; Anticuerpo monoclonal humanizado h-R3: un nuevo concepto terapéutico para el tratamiento del cáncer avanzado; *Biología Aplicada* 2003; Vol.20, No.1
11. Duconge J, Castillo R, Crombet T, Alvarez D, Matheu J, Vecino G, Alonso K, Beausoleil I, Valenzuela C, Becquer MA, Fernández-Sánchez E; Integrated pharmacokinetic-pharmacodynamic modeling and allometric scaling for optimizing the dosage regimen of the monoclonal anti-EGFR antibody; *Eur J Pharm Sci.* 2004; 21(2-3):261
12. Crombet T, Osorio M, Cruz T, Roca C, del Castillo R, Mon R, Iznaga-Escobar N, Figueredo R, Koropatnick J, Rengifo E, Fernández E, Álvarez D, Torres O, Ramos M, Leonard I, Pérez R, Lage A.; Use of the humanized anti EGFR mAb h-R3 in combination with radiotherapy in the treatment of locally advanced head and neck cancer patients.; *J Clin Oncol* 2004 22 (9): 1646
13. Torres LA, Perera A, Batista JF, Hernández A, Crombet T, Ramos M, Neninger E, Pérez M, Sánchez EL, Romero S, Aguilar V, Coca MA, Iznaga-Escobar N; Phase I/II clinical trial of the humanized anti-EGFR monoclonal antibody h-R3 labelled with ^{99m}Tc in patients with tumour of epithelial origin.; *Nucl Med Commun.* 2005; 26(12):1049.
14. Crombet T, Vinageras EN, Ferrer MC, García B, Leonard I, Martínez L, Gonzalez G, Perez R, Lage A. ; Treatment of NSCLC Patients with an EGF-Based Cancer Vaccine: Report of a Phase I Trial.; *Cancer Biol Ther.* 2006; 5:2, 145.
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Grade Glioma Patients with the Humanized anti- EGFR MAb h-R3. Report from a Phase I/II Trial.; *Cancer Biol Ther.* 2006; 5(4):375.

16. Ramos M, Pintado AP, Mesa NR, Oliva JP, Iznaga-Escobar N, Aroche LT, Pimentel G, Gonzalez J, Cordero M, Rodriguez OT, Crombet RT, Perez RR; Diagnostic Efficacy and Safety of (99m)Tc-Labeled MAb Ior c5 in Patients with Colorectal and Anal Carcinomas: Final Report Clinical Trial Phase I/II.; *Cancer Biol Ther.* 2007 Jan 29;6(1)

17. González G, Crombet T, Neninger E, Viada C, Lage A.; Therapeutic vaccination with EGF in advanced lung cancer: analysis of pooled data from three clinical trials; *Hum Vaccin.* 2007;3(1):8

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21. García B, Neninger E, de la Torre A, Leonard I, Martínez R, Viada C, González G, Mazorra Z, Lage A, Crombet T; Effective inhibition of the EGF/EGFR binding by anti-EGF antibodies is related to better survival in advanced non-small-cell lung cancer patients treated with the epidermal growth factor cancer vaccine; *Clin Cancer Res.* 2008 Feb 1; 14(3):840.

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children with high grade glioma with nimotuzumab: a 5-year institutional experience.; *MAbs*. 2013 Mar-Apr;5(2):202-7

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48. Solomón MT, Selva JC, Figueredo J, Vaquer J, Toledo C, Quintanal N, Salva S, Domínguez R, Alert J, Marinello JJ, Catalá M, Griego MG, Martell JA, Luaces PL, Ballesteros J, de-Castro N, Bach F, Crombet T.; Radiotherapy plus nimotuzumab or placebo in the treatment of high grade glioma patients: results from a randomized, double blind trial.; *BMC Cancer*. 2013 Jun 19; 13:299

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63. Saavedra D, García B, Lorenzo-Luaces P, González A, Popa X, Fuentes KP, Mazorra Z, Crombet T, Neninger E, Lage A; Biomarkers related to immunosenescence: relationships with therapy and survival in lung cancer patients.; *Cancer Immunol Immunother*. 2016 Jan;65(1):37-45
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Main Awards:

1997: National award of the Academy of Sciences of Cuba: "EGF vaccine, a therapeutic vaccine for tumors of epithelial origin".

- 2002: July Kieffer Award (Latin American Society of Nuclear Medicine and Radiobiology. Characterization of safety, pharmacokinetic and biodistribution of nimotuzumab in patients with epithelial tumors (Santiago de Chile, Chile, 2002).
- 2003: National Award of the Academy of Sciences of Cuba "AcM h-R3: A new therapeutic concept for the treatment of advanced cancer".
- 2003: National Award for the research work of the greatest scientific relevance of the year.
- 2008: Young Scientist Award in Biology of the Third World Academy of Sciences.
- 2008 Special Award of the Cuban Society of Immunology for the contributions to immunology in Cuba.
- 2009: National award of the Academy of Sciences of Cuba: "Cimavax-EGF, a new vaccine therapy for advanced lung cancer
- 2010: National Award of the Academy of Sciences of Cuba: new evidence on mechanisms of action of nimotuzumab: a new paradigm for the EGFR-targeting therapies.
- 2012: National Award of the Academy of Sciences of Cuba: Nimotuzumab for the treatment of advanced esophageal cancer".
- 2013 National Award of the Academy of Sciences of Cuba: Racotumomab, a new cancer vaccine therapy for advanced lung cancer"
- 2018: Main Award of the Havana City for the contribution to the development of the city.
- 2019: Nation award of scientific innovation: CIMAvax-EGF: novel vaccine for the treatment of lung cancer, which introduces and extends precision medicine in Cuban biotechnology products.
- 2020: 80th Anniversary Medal of the Union of Cuban Workers

2020: Special award of the Ministry of Science for the greatest integration, Novel vaccine for the treatment of lung cancer, which introduces and extends precision medicine in Cuban biotechnology products

- 2020: National Prize for Scientific Innovation in Cuban biotechnology: Repositioning of the Cuban monoclonal antibody itolizumab in the treatment of patients with COVID-19
- 2020 National Award of the Academy of Sciences of Cuba: Repositioning of the Cuban monoclonal antibody itolizumab in the treatment of patients with COVID-19
- 2021: Carlos J Finlay Order: In recognition of extraordinary merits and valuable contributions to the development of the natural or social sciences or to scientific or research activities which have contributed in an exceptional way to the progress of the sciences and to the benefit of humanity, and especially to the preservation and improvement of the health.
- 2021: Chosen by the Academy of Sciences to pronounce the Finlay Prayer on the 188th Anniversary of Finlay's birth.
- 2021. Provincial Prize for Scientific Innovation. Repositioning of the Cuban monoclonal antibody nimotuzumab in the treatment of patients with COVID-19

Patents and other forms of industrial property:

Co-author of the following granted patents:

- Immunotherapeutic combination for the treatment of tumors, Center for Molecular Immunology. Priority Date: December 08, 2000
- Homogeneous vaccine composition comprising a conjugate of EGF and P64K for the treatment of tumors. Molecular Immunology Center. Priority date. June 29, 2012.

Author of 3 new patents in 2020 and 2021, currently under review.

- Use of monoclonal antibodies against the epidermal growth factor receptor in the treatment of patients with acute hypoxemic respiratory failure.
- Use of non-depleting anti-CD6 monoclonal antibodies in the treatment of cytokine storm.
- Use of CiMavax-EGF in the treatment of patients with lung cancer and KRAS mutations.